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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/589,255	06/07/2000	Charles J. Link JR.	P04091US1	8671

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SUITE 3200
DES MOINES, IA 50309-2721

EXAMINER
WEHBE, ANNE MARIE SABRINA

ART UNIT	PAPER NUMBER
1632	

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12

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/589,255	Link
Examiner	**Art Unit**
Anne Marie Wehbé	1632

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Dec 16, 2002* .

2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *19-34* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *19-34* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

A request for continued examination (RCE) under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 12/16/02 has been entered. Also, as requested, applicant's amendment received on 11/19/02 has been entered. Claims 1-18 have been canceled. New claims 19-34 have been entered. Claims 19-34 are pending in the instant application. An action on the merits follows.

Those sections of Title 35, US code not included in this action can be found in the previous office action.

The amendment filed 11/19/02 is objected to under 35 U.S.C. 132 because it introduces new matter into the disclosure. 35 U.S.C. 132 states that no amendment shall introduce new matter into the disclosure of the invention. The added material which is not supported by the original disclosure is as follows: the applicant has amended the claims to recite a "non-gene therapy-based method", the specification does not support the term "non-gene therapy-based".

The applicant is invited to specifically point out where in the specification support for this terminology can be found.

Applicant is required to cancel the new matter in the reply to this Office action.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 19-34 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Applicant's new claims 19-34 introduce new matter into the disclosure of the specification by reciting "non-gene therapy-based" methods which are not supported by the specification, see also above under 35 U.S.C. 132. The specification does not teach "non-gene therapy-based" methods, nor does it define what is meant by a "non-gene therapy-based" method of treating cancer, see also below under 35 U.S.C. 112, second paragraph. The specification teaches the treatment of tumors by the administration of murine retroviral producer cell lines wherein the retrovirus encodes a gene, HSV-TK. Since

the methods disclosed in the specification include the administration of a gene, the specification does not appear to support a "non-gene therapy-based" method of treating cancer. The applicant is invited to specifically point out where in the specification support for this terminology and subject matter can be found.

The rejection of canceled claims 1-16 and 18 under 35 U.S.C. 112, first paragraph, for scope of enablement is maintained over new claims 19-34 for reasons of record as discussed in detail in papers no. 4 and 7. The applicant has not provided any response to these grounds of rejection other than the statement that the cancellation of claims 1-16 and 18 renders the rejection moot. In addition, the applicant has not explained why the new claims are not subject to the same grounds of rejections as the previously pending claims. Applicant's new claims recite subject matter which is substantially similar to the subject matter of the canceled claims. Therefore, the same grounds of rejection are applicable to the new claims, and the rejection of record stands. For clarity of prosecution, the instant grounds for scope of enablement are reiterated below.

The previous office action indicated that the specification, while being enabling for methods of inhibiting the growth of a solid tumor comprising the direct administration to a solid tumor of a xenogeneic retroviral producer cell line which comprises a retrovirus encoding HSV-TK alone or in combination with $\alpha(1,3)$ galactosyltransferase, followed by the administration of gancyclovir, does not reasonably provide enablement for methods of

inhibiting tumor growth comprising the administration of any cell containing α(1,3) galactosyltransferase or the administration of any murine cell line followed by any chemotherapeutic agent.

The applicant claims as written are broad and read on numerous embodiments of the invention which the specification does not enable. In particular, the previous office action stated that the specification does not provide an enabling disclosure for inhibiting tumor growth by the injection/infusion of any type of xenogeneic cells or cells expressing α(1,3) galactosyltransferase to any type of host mammal including humans. It was noted that the specification fails to disclose any means for inducing hyperacute rejection other than the introduction of murine vector producer cell lines which express a retrovirus encoding a gene such as HSV-TK or alpha (1,3)galactosyl transferase to humans. The specification, while demonstrating that murine retroviral producer cells expressing HSV-TK are killed by hyperacute rejection in vivo in patients and that humans cells transduced with alpha (1,3) galactosyltransferase are lysed by human serum in vitro, fails to provide sufficient guidance as to the level of expression of alpha (1,3) galactosyl epitopes or the level of complement activation required to induce hyperacute immune responses in vivo and further to produce a therapeutic immune or innocent bystander effect on local tumor cells. Although the specification and the art at the time of filing disclose that the introduction of xenogeneic cells such as murine or porcine cells to humans results in their rapid destruction by complement fixation or preformed anti-xenogeneic antibodies, neither the art nor the specification

provides any evidence that the destruction of the any xenogeneic cell or xenogeneic viral producer cell in vivo results in any observed tumor treatment in the absence of tk/ganciclovir therapy. In particular, please note that applicant's statement that some effect on malignant ascites was observed following the administration of murine retroviral producer cells encoding HSV-TK before gancyclovir administration does not provide any evidence that the mixed effects observed derived from hyperacute rejection of the murine cells rather than from anti-tumor effects deriving from the expression of TK or from the effects of retrovirus production and infection of tumor cells. Thus, the teachings in the art and the data provided in applicant's specification provide no evidence that hyperacute immune responses to a xenogeneic cell alone are sufficient to induce significant killing of tumor cells.

In addition, in regards to the limitations of new claims 25, 30, and 32-34 which recite methods of inhibiting tumor growth by administering a murine cell followed by the administration of a chemotherapeutic agent, the specification fails to identify any chemotherapeutic agent other than a prodrug activatable by HSV-TK, such as gancyclovir, for use in the instant methods. The specification does not provide any guidance as to the selection of chemotherapeutic agents, or for dosages, routes of administration, or timing between the administration of the murine cells and the chemotherapeutic agent.

Furthermore, the previous office stated that the specification fails to provide guidance for the expression of any genes other than HSV-TK and alpha (1,3) galactosyltransferase in the xenogeneic cells of the instant invention or teach that the expression of any other gene in

a xenogeneic cell results in immune mediated bystander killing of tumors; and that at the time of filing, the art taught that the immunotherapy of tumors using cell based and/or gene based therapies was considered highly unpredictable (Ross et al., Verma et al., and Orkin et al.). Ross et al., Verma et al., and Orkin et al. were cited to establish the state of the art of cell based and gene based therapy of cancer at the time of filing. The combined teachings of these references clearly demonstrate that skilled artisan considered immunotherapy of cancer as unpredictable.

The previous office action also reminded the applicant that 35 U.S.C. 112 requires that the scope of the claims must bear a reasonable correlation to the scope of enablement provided by the specification to persons of ordinary skill in the art. *In re Fisher*, 166 USPQ 18, 24 (CCPA 1970). Previous office actions analyzed the specification in direct accordance to the factors outlined in *In re Wands*, namely 1) the nature of the invention, 2) the state of the prior art, 3) the predictability of the art, 4) the amount of direction or guidance present, and 5) the presence or absence of working examples, and presented detailed scientific reasons supported by publications from the prior art for the finding of a lack of enablement for the instant methods. In addition, case law including the Marzocchi decision sanctions both the use of sound scientific reasoning and printed publications to support a holding of non-enablement (see *In re Marzocchi* 169 USPQ 367, and *Ex parte Sudilovsky* 21 USPQ2d 1702). Further, the unpredictability of a particular art area may alone provide reasonable doubt as to the accuracy of the broad statement made in support of enablement of claims. See

Ex parte Singh, 17 USPQ2d 1714 (BPAI 1991). Ultimately, case law states that ".. the disclosure of an application shall inform those skilled in the art how to use applicant's alleged discovery, not to find out how to use it for themselves." *In re Gardner* 166 USPQ 138 (CCPA) 1970. Thus, having properly analyzed the specification in accordance to the factors identified in *In re Wands*, the office has concluded that in view of the art recognized unpredictability of inducing therapeutically effective anti-tumor immune responses in vivo, the lack of guidance provided by the specification for means of inducing a hyperacute response in any mammal other than the administration of murine viral producer cells which express HSV-TK or viral producer cells which express HSV-TK and alpha (1,3) galactosyltransferase, the lack of guidance concerning vector/gene selection such that the level of induced hyperacute immune responses in vivo correlates with tumor killing, the limitation of the working examples to the administration of murine vector producer cells which produce a retrovirus encoding HSV-TK, and the breadth of the claims, it would have required undue experimentation to practice the scope of the invention as claimed and the skilled artisan would not have predicted success in inhibiting tumor growth in a human by administering murine cells which are not retroviral producer cells expressing TK, or by administering any cell which expresses alpha (1,3) galactosyltransferase.

The rejection of claims 6-8 and 15-16 under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, is withdrawn in view of applicant's cancellation of the claims.

Claims 19-34 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. New claims 19-34 recite a "non-gene therapy-based method" for inhibiting tumor growth. The specification does not recite the phrase "non-gene therapy based" or provide a definition of a "non-gene therapy-based" method. Based on applicant's claims 33-34, it appears as though the "non-gene therapy-based" method can include the administration of cells which produce recombinant retroviruses and which encode genes. At the time of filing, the term "gene therapy" encompassed any methodology wherein a recombinant gene was introduced into an animal for the purpose of disease treatment. Based on the fact that the "non-gene therapy-based" methods appear to include the administration of cells which express heterologous genes and which can produce recombinant vector, the metes and bounds of the phrase "non-gene therapy-based" cannot be determined.

Double Patenting

The rejection of canceled claims 1-4, 6-12, and 15 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 4 and 7 of U.S.

Patent No. 5,869,035, hereafter referred to as the '035 patent, is maintained over new claims 19-24 and 26-29. The applicant has not provided any arguments in response to this double patenting rejection other than the statement that the cancellation of claims 1-4, 6-12, and 15 renders this rejection moot. In addition, the applicant has not explained why the new claims are not subject to the same grounds of rejections as the previously pending claims. As the subject matter of claims 19-24 and 26-29 is substantially similar to the subject matter of claims 1-4, 6-12, and 15, the rejection of record stands.

It is noted that the applicant stated in the response submitted on 6/18/02 that a terminal disclaimer over U.S. Patent No. 5,869,035 has been submitted to the office. However, a terminal disclaimer over U.S. Patent No. 5,869,035 has never been received. If applicants have in fact submitted such as document, the office requests that a copy be provided for entry into the instant record. In view of the fact that a terminal disclaimer is not of record in the instant case, the double patenting rejection and concurrent rejection of the claims under 35 U.S.C. 102(e) has been maintained.

Claims 19-24 and 26-29 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 4 and 7 of U.S. Patent No. 5,869,035, Feb. 9, 1999, hereafter referred to as the '035 patent. As noted in previous office actions, although the 5,869,035 patent and the instant application are commonly assigned to the Human Gene Therapy Research Institute, the inventive entities of the two are different. The '035 patent lists Charles J. Link, Jr. and John P, Levy as inventors whereas the

instant application lists Charles J. Link , Jr. and Tatiana Seregina. Therefore, in view of the different inventorship, the above claims have been rejected over the '035 patent under both obviousness-type double patenting and 35 U.S.C. 102(e), see below.

Although the conflicting claims are not identical, they are not patentably distinct from each other for the following reasons. The '035 claims recite broad methods of killing tumors comprising delivering to said tumor cells a vector producer cell line with a polynucleotide sequence that comprises a recombinant HSV plasmid vector that expresses α(1,3) galactosyltransferase. The '035 claims are broad and do not specifically recite the species of the vector producer cells or the species of the host. However, the '035 specification teaches that the preferred host is an old world monkey or human which does not express α(1,3) galactosyl epitopes and that the preferred vector producer cell line is a murine cell line (the '035 patent, column 3, and column 7, lines 1-6). The '035 specification also teaches that tumor to be treated include ovarian tumors and tumors located in the peritoneum (the '035 patent, column 11, lines 25-67 and column 12, lines 1-3). Therefore, while the '035 claims are broader than the instant claims, the '035 patent clearly teaches all the recited limitations of the instant claims and as such renders the instant claims obvious.

Claim Rejections - 35 USC § 102

The rejection of canceled claims 1-4, 6-12, and 15 under 35 U.S.C. 102(e) as being anticipated by U.S. Patent No. 5,869,035, hereafter referred to as the '035 patent, is

maintained over new claims 19-24 and 26-29. The applicant has not provided any arguments in response to this rejection other than the statement that the cancellation of claims 1-4, 6-12, and 15 renders this rejection moot. In addition, the applicant has not explained why the new claims are not subject to the same grounds of rejections as the previously pending claims. As the subject matter of claims 19-24 and 26-29 is substantially similar to the subject matter of claims 1-4, 6-12, and 15, the rejection of record stands.

As noted above, the terminal disclaimer referred to by the applicant's has not been received by the office. As such, it cannot be relied upon to overcome the instant grounds of rejection.

The '035 patent teaches methods of killing tumors comprising delivering to said tumor cells a vector producer cell line with a polynucleotide sequence that comprises a recombinant HSV plasmid vector that expresses α(1,3) galactosyltransferase ('035 patent, claims 4-7). The '035 specification further teaches that the preferred host is an old world monkey or human which does not express α(1,3) galactosyl epitopes and that the preferred vector producer cell line is a murine cell line (the '035 patent, column 3, and column 7, lines 1-6). The '035 specification also teaches that tumor to be treated include ovarian tumors and tumors located in the peritoneum (the '035 patent, column 11, lines 25-67 and column 12, lines 1-3). Therefore, by teaching all the limitations of the claims, the '035 patent clearly anticipates the instant invention.

The rejection of canceled claims 1, 3-4, 6, 9-12, and 15-16 under 35 U.S.C. 102(e) as being anticipated by U.S. Patent No. 6,045,789, hereafter referred to as Culver et al., is maintained over new claims 19-34. The applicant has not provided any arguments in response to this rejection other than the statement that the cancellation of claims 1-4, 6-12, and 15 renders this rejection moot. In addition, the applicant has not explained why the new claims are not subject to the same grounds of rejections as the previously pending claims. As the subject matter of claims 19-24 and 26-29 is substantially similar to the subject matter of claims 1-4, 6-12, and 15, the rejection of record stands.

The applicant new claims recite methods of inhibiting tumor growth in a human comprising the delivery to a tumor of cells containing $\alpha(1,3)$ galactosyl epitopes. The applicant further claims said methods wherein the cells are murine cells, wherein the tumor is a solid tumor selected from a group which includes ovarian carcinomas, and wherein the administration of the cells is followed by administration of a chemotherapeutic agent. The applicant also claims said methods wherein the cells are murine retroviral vector producer cell line, and wherein the retroviral vector is derived from Moloney murine leukemia virus.

Culver et al. teaches the injection of a murine retroviral packaging cell line which produces a retrovirus encoding HSV-TK to a solid tumor in a subject resulting in tumor treatment following ganciclovir administration (Culver et al., column 13, lines 39-57, and column 14, lines 1-14, and claims 1-5). Culver et al. teaches that the intended subject for the

disclosed method is a human cancer patient (Culver et al., columns 1-2). Culver et al. further teaches that the administration of the murine HSV-TK retrovirus producing cell to the tumor resulting in bystander killing of tumor cells which do not express HSV-TK (Culver et al., see for instance columns 4). While Culver does not explicitly teach that the murine cells express α(1,3) galactosyl epitopes, it is an inherent property of murine cells that they utilize α(1,3) galactosyltransferase in protein glycosylation and that murine proteins contain α(1,3) galactosyl epitopes. In addition, Culver teaches that the disclosed method is useful for treating a number of solid tumors including ovarian tumors (Culver et al., column 10, 13-21). Thus, Culver teaches the treatment of tumors comprising the administration of xenogeneic murine retrovirus producing cells directly to a tumor in a subject which includes humans wherein the murine cells produce a retrovirus which encodes HSV-TK and IL-2 such that an immune response is generated against the tumor and that tumor cells are also killed directly by HSV-TK/ganciclovir or indirectly by innocent bystander effect. By teaching all the limitations of the claims, Culver et al. anticipates the instant invention as claimed.

The applicant is reminded that the office does not have the facilities for examining and comparing applicant's cells murine retroviral producer cells with the murine retroviral producer cells of the prior art in order to establish that the product of the prior art does not possess the same material, structural and functional characteristics of the claimed product. In the absence of evidence to the contrary, the burden is upon the applicant to prove that the claimed products are functionally different than those taught by the prior art and to establish

patentable differences. See Ex parte Phillips, 28 USPQ 1302, 1303 (BPAI 1993), In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and Ex parte Gray, 10 USPQ2d 1922, 1923 (BPAI 1989).

The rejection of canceled claims 1-4, 6-12, and 15 under 35 U.S.C. 102(a) over Klatzmann et al. is maintained over new claims 19-34. The applicant has not provided any arguments in response to this rejection other than the statement that the cancellation of claims 1-4, 6-12, and 15 renders this rejection moot. In addition, the applicant has not explained why the new claims are not subject to the same grounds of rejections as the previously pending claims. As the subject matter of claims 19-24 and 26-29 is substantially similar to the subject matter of claims 1-4, 6-12, and 15, the rejection of record stands.

The applicant new claims recite methods of inhibiting tumor growth in a human comprising the delivery to a tumor of cells containing $\alpha(1,3)$ galactosyl epitopes. The applicant further claims said methods wherein the cells are murine cells, wherein the tumor is a solid tumor selected from a group which includes ovarian carcinomas, and wherein the administration of the cells is followed by administration of a chemotherapeutic agent. The applicant also claims said methods wherein the cells are murine retroviral vector producer cell line, and wherein the retroviral vector is derived from Moloney murine leukemia virus.

Klatzmann et al. teaches the treatment of melanoma tumors in humans by direct intratumoral injection of a xenogeneic murine retroviral producing cell line that produces a

retrovirus encoding HSV-TK followed by the administration of ganciclovir (Klatzmann et al., page 2585). While Klatzmann et al. does not explicitly teach that the murine retroviral producer cells express α(1,3) galactosyl epitopes, it is an inherent property of murine cells that they utilize α(1,3) galactosyltransferase in protein glycosylation and that murine proteins contain α(1,3) galactosyl epitopes. Klatzmann et al. observed local inflammatory reactions at the tumor site following the injection of the xenogeneic cells and specifically states that the transplanted murine cells are rejected within 7-10 days as a result of hyperacute rejection mediated by preformed antixenogeneic antibodies and complement (Klatzmann et al., page 2585, abstract). Thus, it would appear that the ability of xenogeneic murine retroviral producer cells which produce a retrovirus encoding HSV-TK to generate hyperacute immune responses in a human which result in innocent bystander killing of tumor cells is an inherent property of the xenogeneic murine retroviral producer cells. Thus, by teaching all the limitations of the instant methods, Klatzmann et al. anticipates the invention as claimed.

The applicant is reminded that the office does not have the facilities for examining and comparing applicant's cells murine retroviral producer cells with the murine retroviral producer cells of the prior art in order to establish that the product of the prior art does not possess the same material, structural and functional characteristics of the claimed product. In the absence of evidence to the contrary, the burden is upon the applicant to prove that the claimed products are functionally different than those taught by the prior art and to establish patentable differences. See Ex parte Phillips, 28 USPQ 1302, 1303 (BPAI 1993), In re Best,

562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and Ex parte Gray, 10 USPQ2d 1922, 1923 (BPAI 1989).

Claim Rejections - 35 USC § 103

The rejection of claims 1, 3-6, and 9-17 under 35 U.S.C. 103 over U.S. Patent No. 6,045,789, hereafter referred to as Culver et al. in view of Link et al., and further in view of Levy et al. is withdrawn in view of applicant's cancellation of the claims.

No claims are allowed.

Any inquiry concerning this communication from the examiner should be directed to Anne Marie S. Wehbé, Ph.D., whose telephone number is (703) 306-9156. The examiner can be reached Mon-Fri from 10:30-7:00 EST. If the examiner is not available, the examiner's supervisor, Deborah Reynolds, can be reached at (703) 305-4051. General inquiries should be directed to the group receptionist whose phone number is (703) 308-0196. The technology center fax number is (703) 308-4242, the examiner's direct fax number is (703) 746-7024.

Dr. A.M.S. Wehbé

ANNE M. WEHBE' PH.D
PRIMARY EXAMINER